PANEL: METHODOLOGY & INSTRUMENTATION

MANDATE:
To examine the means by which schizophrenia research is carried out, specifically the instruments that are used in the evaluation of the illness and its treatment.
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INTRODUCTION

There is a general agreement among Canadian researchers in the field of schizophrenia that they are investigating a heterogeneous set of disorders. To encompass all of the diversity in the etiology and to move forward in the treatment management of this disease, it is crucial to identify sub-types or categories within the symptomatology and to agree upon commonly recognized markers to accompany this criteria.

To initiate the desired commonality in approach to this heterogeneous disease, investigators are determined to develop a comprehensive collection of useful tools to employ in their discussions of the disease. The Methodology and Instrumentation Panel will be involved in the evaluation and promotion of agreed upon assessment tools and outcome measures.

It is important to note at the outset that this panel is not expected to dictate the tools of research but to engage in research into the components and contributions of various instruments and methodology techniques, and to make recommendations about various tools and instruments.

CURRENT RESEARCH PROFILE

Knowledge Status

In recent years, there has been a concerted attempt to determine the homogeneous qualities of this disease. It is fairly well accepted that schizophrenia exists in more or less consistent forms in all cultures. The need and the temptation to validate this belief and to extract from it the dissimilari-
ties is mounting as evidence accumulates about the differing effective treatments within cultures.

There has also been growing discontent with the strict categorization of positive and negative symptoms and their connection to brain physiology and to the course of the illness. A third category of symptoms referred to as "disorganized" has emerged.

Various associations with the age and gender of the patient have been relatively well accepted among researchers. It would appear that males show an earlier onset and that they have a more chronic course. The reasons for these differences that have been assumed, consider the impact of both psychological and biological influences, and include the estrogen down regulation of dopaminergic activity of the brain. There have also been predictions of the course of the illness based on the age of onset (the earlier, the less likely a benign course). What is clear is that more studies on the prevalence and the incidence aspects of this disease, and those associated factors, need to be done within the Canadian setting.

Most authorities now accept the hypothesis of genetic vulnerability in schizophrenia, but it is also acknowledged that only about ten per cent of diagnosed schizophrenics have a positive family history for the illness. The application of common tools to the field of genetic linkage analysis would encourage the sharing of information and would reveal more about the inherited vulnerability to illness and the complex interaction, during the chronic course of this disease, between predisposition and environmentally induced risk. This kind of involved investigation of the nature of risk and its mitigating factors of cause and effect, is best done within the context of longitudinal studies with a

multi-disciplinary disposition and a multi-centre locus. Such simultaneous and comprehensive studies also require the inclusion of shared definitions as well as assessment tools and outcome measures.

While some studies have been done to demonstrate the relevance of the incidence and prevalence of the disease, there is a general feeling that fewer cases are being misdiagnosed.

More studies need to be done into this crucial issue of timing and accuracy in diagnoses - especially within the confines of the Canadian population.

Several factors appear to influence the incidence (the number of new cases within a given period) including the following: the determination of the family to seek help which may be culturally biased, the availability of appropriate and acceptable care, the careful application of diagnostic criterion, the gender of the patient and that patient's symptom manifestation (if males are more aggressive in their psychotic break families may more immediately seek help - another potentially culturally oriented response), and the perceived effectiveness of medication.

Strengths of Canadians Research

Canada has a number of researchers who are interested in the cooperative aspects of investigation that would contribute to the discussion and eventual implementation of assessment tools and outcome measures in common. The aspects of the disease that such joint approaches would benefit in terms of collection and compilation of data include the following: diagnosis of the illness, including the date and precipitating causes of the onset, the stages of manifestation of the disease, the severity of the illness, the neurocognitive assessment during both the diagnosis and the course of the disease, and the functional status of the patient at various junctures.

The formation of CAROS provides the appropriate administrative support structure to recommend the sharing of assessment tools and outcome measures to ensure collegiality and Canada-wide acceptance of careful and consultative research into effective investigative and treatment methodologies. CAROS facilitates the comparison and validation of studies while actively pursuing a multi-disciplinary and multi-centre approach to such studies.

There is, within the Canadian research community, a strong sense of the need to establish and maintain an active database of Canadian incidence and prevalence information. It is not intended that such a database would confine itself to statistical information, but would include descriptive information in a common format about the age and determination of onset.

It is also felt that such a database that was amplified by other relevant information about the longitudinal course of the illness in a structured form, and which included family and personal history, would be an added attraction to recruit new researchers to this field. The implementation of such a complete and uniform database would provide the next generation of researchers with a wealth of information and suggestions of future orientations in research.

Finally, Canadian researchers who are interested in the research aspects of the development of common assessment tools and outcome measures are aware and supportive of active consumer involvement in the design of such tools and measures. The incorporation of the subjective experience is regarded as integral to the definition and elaboration of any "quality of life" measures.

Deficiences of Research

Researchers who have been involved in the field for a number of years have developed preferences for specific existing research instruments which may appear to be especially relevant for their area of expertise. For example, the epidemiologists may prefer the DIS, the psychosocial researcher may use the SADS, and the more biologically oriented researcher may automatically adopt the SCID. It is the task of this panel to exhaustively research all tools in current use and to deliver credible recommendations about the effective, mutual use of existing tools, and to design, by consensus, additional tools for common use.

To be convincing in its mandate, this panel is required to make the best use possible of the limited and distributed Canadian resources in the area of the neurological sciences and imaging techniques. It is important that there be extensive cooperation between this panel and the Neurobiology and Imaging Panel, which can be facilitated through the ongoing existence of CAROS.

The viability of CAROS is also essential to support the communal discussion and future adoption of specifically recommended research instruments. CAROS may provide a more objective overview of appropriate instrumentation for schizophrenia research than the pharmaceutical industries which now exert a strong influence on some measures, in conjunction with regulatory bodies like the Health Protection Branch. CAROS could, through the joint effort of the Psychopharmacology Panel and the Instrumentation Panel, promote cooperation in this area with industry and government.

Under the auspices of CAROS, the development of a comprehensive and consistent database for the Canadian scene can be initiated and nurtured. Inroads will have to be made into the legal tangles of confidentiality to ensure that any database or patient registry has been designed with sufficient precautions for both security and ethical considerations. There is an obvious need here to incorporate the consumer perspective as well as their legally acknowledged rights. This will be a complex interaction that has no substantial precedent in the Canadian setting.

FUTURE RESEARCH OPPORTUNITIES

Capitalization on Existing Resources

In Canada there exists a population of researchers with the skill and dedication necessary to conduct beneficial and effective research into the many aspects of the etiology and treatment of this disease. Many of these investigators are also keenly interested in the development of common tools of assessment and outcome measure.

The consumer and family community is also supportive of the development and implementation of appropriate and heuristic methods of conducting research in common. The consumer is especially galvanized to contribute to the inclusion and expansion of the subjective experience in relation to quality of life indicators. The family community can provide valuable information about the family history, not only of the disease occurrences but also of course of illness patterns. The involvement of the family and consumer communities will ensure the research consideration of such contributing factors as life events and social relationships or networks to the onset and course of the disease.

The presence of regionally located, large families demonstrating the genetic vulnerability to schizophrenia contributes to a rich base of information for the inclusion of family data, using scales in common with other strategies as appropriate. If research centres work together, this is just one area where shared information in a universally accepted format would provide a statistical database of sufficient patterns of markers or illness variables.

There is a rich multi-cultural milieu in which to investigate the many considerations in research related to the cultural origins or influences of those affected by the disease. Canada has the population heterogeneity to encourage and facilitate studies into the culturally differential responses to disease onset, the seeking of treatment and the response to neuroleptics, just to name a few potential research areas.

Any studies into disease incidence and prevalence in Canada will be enhanced and assisted by access to the documentation currently available through the different provincial medicare systems. One such focus for this currently accumulating information could be the dual dating of illness onset. One date of importance is the onset of the prodromal phase, distinguished by social withdrawal. The second date of importance is the initiation of the active phase, marked by the emergence of positive symptoms such as hallucinations. There is also a body of knowledge to tap into concerning appropriate and secure methods of collecting concomitant medical data.

The close connection between researchers and clinicians in Canada will also ensure that the applicability of the research protocols or results can be more readily assimilated into the therapeutic clinical setting. This interdependent relationship is also fundamental to the shared sense that the disease liability concept is best viewed as a continuum of vulnerability to ensure that there is no premature closure on the complex study of the disease etiology.

Involvement of Consumer Concerns

As has been mentioned earlier in this report, it is absolutely essential to incorporate the consumer (patient) viewpoint on the quality of life indicators included in any assessment or outcome scale. It may be that there will have to be additional research applied in the area of interaction with, and support of, consumers involved in this level of research. This is perhaps best demonstrated by the current general lack of consensus in good quality of life instruments for schizophrenia.

To ensure that individual histories are revealing and accurate, researchers will interact with consumers to develop precise and universally understood questions for any scale under development.

Consumer participation is essential to provide the opportunity to incorporate all influences, both biological and psychological, with regard to instruments of both assessment and outcome. For instance, the charting of family histories or social interactions can not be incorporated into any assessment tool without the active consent and cooperation of consumers.

Consumers should also be involved in the necessary considerations regarding informed consent and the security of confidential information. The development of a comprehensive database is essential to the work of this panel, but the legitimate concerns of the consumers regarding the ethical considerations of the exchange of personal information must be incorporated into any future plan.

The issue of risk management will be better understood by researchers designing or utilizing this aspect of a particular instrument if there is an opportunity to investigate the connection between genetic vulnerability and pre-onset stressors, as verbalized by the patient. This discussion may result in better treatment strategies to address the relapse concern.

Enhancement by Multi-centre Approach

In order to effectively recommend existing scales or to design more specific or operationally superior tools of assessment and outcome, this panel must excel at comprehending the nature of the research and the interaction of researchers in the various research and clinical centres across Canada.

It is essential to pull into these considerations the neurobiological and imaging studies that are currently being performed in various Canadian research settings. The realistic ambitions of these researchers to enhance their programs by incorporating the latest technology should also be of interest

to this panel as it continues to recommend better assessment tools.

Multiple centres not only offer differential expertise in terms of the various components of a particular scale as it is being reviewed or developed, they also offer, individually and jointly, unique settings for the testing, validation, or appropriate replication of new approaches.

The proposed introduction of a new scale in a variety of research and clinical settings will have greater credibility, and appeals with both the subject population and the research community when it is clear that it is endorsed across the country. With the involvement of many centres in the formulation of new scales there will be increased opportunities to employ useful comparison samples of differing control compositions, as well as differing sub-groups within the illness.

The development and maintenance of a comprehensive database on schizophrenia in Canada will be strengthened by the collaboration of many centres of ongoing activity in this regard. In addition to contributing to the power of the statistical database, this will also contribute to the attraction of international attention toward Canadian research enterprise in this area. Of course, where scales have achieved international consensus as appropriate measures of a given area, then these can be adopted and recommended for use in Canadian strategies.

Needed Resources

Funding is required to bring together researchers within the panel and from all interested areas of research identified by the six panel composition of CAROS. Within this multidisciplinary context of collaboration, a review of existing scales and tools of research can be launched. Some of the expert input required from research, academic, and clinical settings includes the responses of therapists and consumers to the effectiveness and utility of scales in common use such as:

Symptom Scales

- the BPRS (Brief Psychiatric Rating Scale) the PANSS (Positive and Negative Symptom Scale) the SANS and the SAPS (Scales for the Assessment of Negative [Positive] Symptoms)

Diagnostic Interview Schedules

- the SCAN (Schedule for Clinical Assessment in Neuropsychiatry) the CIDI (Composite International Diagnostic Interview) the PSE (Present State Examination)

Social Functioning Measures

- the Philips Scale the SPI (Social Performance Index)

Side Effect Scales

- the ESRS (Extraprymidal Symptom Rating Scale) the AIMS (Abnormal Involuntary Movement Scale)

The starting point in any discussion of a particular group of scales or measures would be to identify the core components of assessment for all patients, versus extended components for subgroups of patients. The core components might include:

- basic demographic information, preferably gathered in a compatible manner to medicare and Statistics Canada models,

- the first noticeable signs of the onset of the illness as detectable by both deteriation and dysfunction, as well as the onset of outright psychotic symptoms,

- life events, realizing problems of recall, focus and ordering,

- the delineation of positive, negative, and disorganized symptoms,

- the measurement of side effects of drugs

- the family history of mental illness,

- the charting of social relations or networks including pre-morbid and current trends,

- physical health and development issues such as obstetrical complication, and viral infection during pregnancy.

The above is by no means meant to be an inclusive list of considerations, but was designed to point out the complicated nature of assessment methodologies in this complex illness. It is also assumed that in the case for the consumer as a needed resource to this panel has already been made clear, as has the need to develop a research database to substantiate these studies and to attract new researchers.

Realistic Goals

In the isolation of even one component of an assessment scale, it is evident that considerable research must be done to ensure that the multi-disciplinary aspects of the proposed methodology and the acknowledged complex nature of this disease, with its enmeshed interactions of biological and psychological factors, are thoroughly investigated. As a case in point, let us briefly review aspects of the CIDI.

One of the attractions of this diagnostic interview is its orientation toward the subject's self assessment as opposed to the determination of the interviewer. Because of its semi-structured format, it can be administered by lay interviewers and can be effectively scored by computer in large epidemiological studies. It is a relatively sensitive instrument with a

good review of lifetime events. However, one of the goals of this research panel would be to assess the efficacy of this scale from many points of view including, for instance, its sensitivity to the social development of the client.

Now let us explore, hypothetically, prospective panel deliberations about a novel scale to delineate concepts in the area of social accomplishments. In the first instance, let us assume that one goal was to assess for attainment. The method of assessing for that would have to be established - perhaps by the calculation of the number of people that he/she could count on. Other factors of assessment might include the social status of the family, evidence of transience, or employment or education accomplishments.

Perhaps another goal would be to assign a performance rating in this context. This might be done by eliciting information about social adjustments or social role performance in a variety of settings including the family, the work place, or the community environment. The third area of assessment could be in the area of satisfaction. This determination would require subjective reporting of the qualitative aspects of well-being.

One of the obvious goals of this research panel must be to identify what it is important to know and then to determine the most likely way of obtaining reliable and relevant responses.

Another goal must be the incorporation of the subjective experience in a way that promotes optimal consultation and the absolutely essential security of confidential information.

Ultimately, this panel would like to establish research instruments that exemplify the best case-identification methods and contribute uniform definitions to the body of knowledge about effective assessment tools in this heterogeneous disease.

In addition to assessing or creating such diagnostic tools, it is imperative that this panel engage in longitudinal studies in order to relate the study of the course of the illness to the original diagnosis or even prognosis. There is much to be gained in the understanding of onset and relapse in the context of such studies, provided developmental, family, social, neurological, pharmacological and subjective response issues are carefully delineated by the research instruments of choice.

With a common, minimum set of research instruments used in every study with schizophrenia patients, a database of comparative studies in a variety of Canadian settings could be established and continually enriched.

If researchers continue to investigate and document their studies by common methods of conceptualization, and with an open mind regarding the complexity of this illness, there will be no danger that a rigidity of diagnostic tools will set in. This flexibility is essential if new symptoms and influences are to be identified and included in the diagnostic scheme. In addition to assessing for symptoms, researchers must also be encouraged to look beyond the initial diagnosis

to the resultant disability, to chart the course and the ebb and flow in the severity of the illness, and to be vigilant about the inclusion of co-morbidity in their longitudinal view of assessment.

Any tools that are recommended for universalized use within Canada must have the support of clinicians within Canada and must also meet international standards of accomplishment and acceptability.

INTERACTION OF THE PANELS

It is the intent of this panel to provide valuable assistance to its fellow panels concerning the identification and review of appropriate and intelligent research tools. It is a mutually beneficial relationship, since the most effective research tools will emerge from a collaborative effort to identify the most salient features of a proposed scale.

What all panels have in common at the outset is the determination to deal with this heterogeneous disease from a multi-disciplinary vantage point. Thus all panels start out with a vested interest in the inclusion of all panels' areas in the design of assessment and outcome instruments.

All the panels also have in common the articulated desire to interact throughout the course of invaluable longitudinal studies. Such studies would allow for a thorough investigation of the interrelationship between the biological and psychological environment factors and genetic vulnerability.

This panel also has the opportunity to put into effect the expressed need of all panels to incorporate consumer concerns and input into appropriate vehicles for expression.

Overall the support that this panel will provide to multi-disciplinary research involving complementary scientific paradigms, will promote and enrich a science of increasing complexity and growing Canadian perspectives.

CONCLUSION

It is probably fair to say that, to a large extent, the secure underpinning of the interaction of all the panels within CAROS will depend upon the credible and consultative work done by the Instrumentation and Methodology Panel. It is within this arena that researchers from different disciplines and various centres will have to interact and collaborate in a tangible way to realize their aspirations for Canadian designed research instruments, and Canadian standardized research measurement.

It would be naïve to assume that one panel can impose formats on any other without incurring animated discussion. The object is to reach a consensus that will allow for the initiation and continuation of a database within Canada for researchers to use to broaden their insight and their approach to research methodologies in an illness that threatens to swamp the novice with its many configurations and too often discouraging course of chronicity.

In the process of this methodical but far ranging information gathering, it is hoped that the sub-groups of symptom configurations of the illness will be illuminated - not just by researchers but by the alliance with consumers and family members in the cause of clarifying the etiology of this disease.

Research Needs and Priorities

Since research on methodology and instrumentation is really only effective as part of broader research strategies, the panel has made recommendations of a general nature,

which would be helpful in research proposed by other panels:

- Funding agencies should allow additional funds for schizophrenia studies to ensure uniform and standardized measurements are used;

- Funded researchers should be encouraged to call upon expert opinion to recommend instruments and measures based on type of research planned; and

- Support studies are needed that include assessment of the quality of life, especially those obtained from the consumer's point of view.

Instrument Comparison Table

	DIS	SCID	CIDI	PSE-9
Reliability	High	Might be poor	High	Might be poor
Validity	Questionable	Good face validity	Poorer than PSE-9 but better than DIS	Good face validity
Interviewer	Trained by lay person	Trained clinician experienced with population	Trained lay person	Trained clinician experienced with population
Time to administer	1-3 hours	1-3 hours	1-3 hours	1-3 hours
Data source	patient only	all available sources	patient only	all available sources
Period under study	Current episode and lifetime prevalence	Past month and past episodes	Current episode and lifetime prevalence	Previous month and past episode if appendix used
Questions	Closed	Open, then closed	Closed	Open, then closed
Structure of Interview	Non clinical No overview Present / absent	Overview module Present/ absent	Non clinical No overview Present /absent	Clinical interview
Diagnoses	Feigner, RDC, DSM- III	DSM-III-R	DSM-III-R	ICD-9, DSM-III
Method of diagnosis	Computer, after interview	Interviewer, during interview	Computer, after interview	Computer, after interview or interviewer after interview
Ease of Use	Research assistant	Clinician	Research assistant	Clinician
Training	Extensive Available in Toronto	2x12 hour/days & homework $2400 & expenses	Extensive Available in Toronto	Extensive Available in Toronto
Computerized Version	Yes	Yes	Yes	Yes
Other comments				

INSTRUMENT SUMMARY

DIS

Advantage
An epidemiological field instrument Reliability high, very structured, good for lay person. Has been translated into different languages. Widely used in North America

Disadvantage
Validity may be poor because scoring dependent upon patient self report - limits on clinical judgement.[2]
Application limited in a chronic psychotic population. Diagnosis made is lifetime not necessarily present condition. Weak in terms of evaluating anxiety, personality disorder and phobias. Over representative of affective disorders.[2]

SCID

Advantage
Allows for clinical judgement.
Information comes from all available sources Validity high (Brenda Toner: personal communication). Adapted for DSM-III-R diagnosis Axis II (personality disorder diagnosis available). Wider range of diagnosis than DIS.

Disadvantage
Reliability may be poor (Brenda Toner: personal communication) Used in several personality disorder studies. There has been very little work published on its reliability and validity.

CIDI

Advantage
Highly structured epidemiological instrument for lay person. Good reliability. Developed from DIS and includes 63 items from PSE-9. A severity scale has been added for each question.[3,5]

Disadvantage
Performs better for definite cases than marginal cases.[3]

PSE-9

Advantage
Good face validity. Widely used in Europe.

Disadvantage
Reliability not as good as CIDI while its validity is better. A lot of modifications have been done since 1973 to incorporate into DSM-III-R -(e.g. better definitions of some items, extra rating points added to the three- point scales of severity). SCAN (PSE-10) is available now.[6] (The European Science Foundation makes use of the PSE-10 and the SADS-L in the Molecular Genetics of the Major Psychoses to ensure reliability across centres).[7] Not used in North America to a great degree.

DIS   Diagnostic Interview Schedule
SCID   Structure Clinical Interview for DSM-III-R
CIDI   Composite International Diagnostic Interview (Core Version #1 November 1990)
PSE-9   Present State Examination (9th Edition - 10th available)

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